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#4	Search (pharmaceutical) AND ("GPR65" [TIAB] OR "GPR-65" [TIAB] OR "GPR 65" [TIAB] OR "G-protein coupled receptor 65" [TIAB] OR "hTDAG8" [TIAB] OR "hTDAG-8" [TIAB] OR "hTDAG 8" [TIAB] OR "Psychosine receptor" [TIAB] OR "T cell-death associated protein 8" [TIAB] OR "TDAG8" [TIAB] OR "TDAG-8" [TIAB] OR "TDAG 8" [TIAB])	18:56:10	<u>0</u>
#3	Search (camp) AND ("GPR65" [TIAB] OR "GPR-65" [TIAB] OR "GPR 65" [TIAB] OR "G-protein coupled receptor 65" [TIAB] OR "hTDAG8" [TIAB] OR "hTDAG-8" [TIAB] OR "hTDAG 8" [TIAB] OR "Psychosine receptor" [TIAB] OR "T cell-death associated protein 8" [TIAB] OR "TDAG8" [TIAB] OR "TDAG-8" [TIAB] OR "TDAG 8" [TIAB])	18:55:50	<u>3</u>
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Symbol	Name	Synonyms	Or
 GPR65	G protein-coupled receptor 65	G-protein coupled receptor 65, hTDAG8, Psychosine receptor, T cell-death associated protein 8, TDAG8	Ho
UniProt	Q8IYL9, O75819		
OMIM	604620		
NCBI Gene	8477	more than 1,500 organisms. 80,000 genes. 12 million sentences. ...always up-to-date	
NCBI RefSeq	NP_003599		
NCBI RefSeq	NM_003608		
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


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

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


2. Furthermore, **RhoA** activation and actin rearrangement were elicited by acid-stimulated **TDAG8** . [2005]

G protein [?]-coupled receptors **GPR4**  and **TDAG8**  are oncogenic and overexpressed in human cancers. [


The subfamily of **G protein-coupled** receptors comprising **GPR4** , **OGR1** , **TDAG8** , and **G2A**  was originally characterized as a group of proteins mediating biological responses to the lipid messengers **sphingosylphosphorylcholine (SPC)**, **lysophosphatidylcholine (LPC)**, and **psychosine**. [2006]

Here we show that **GPR4**  also malignantly transforms NIH3T3 cells and that **TDAG8**  malignantly transforms normal mammary **epithelial cell** line NMuMG. [2004]

G2A , **T cell** death-associated gene 8 (**TDAG8** [?] ) , **ovarian cancer G protein-coupled receptor 1**  (**OGF G protein-coupled receptor 4** [?] ) (**GPR4** ) form a group of structurally related G protein-coupled receptors (originally proposed to bind proinflammatory lipids. [2005]

Receptors of the endothelial differentiation gene family are activated by **S1P** [?] (S1P(1-5)) or **LPA** (LPA(1-3)); two distantly related receptors are activated by **LPA** (LPA(4/5)); the GPR(3/6/12) receptors have a high constitutive activity and are further activated by **S1P** [?] and/or **SPC**; and receptors of the **OGR1**  cluster (**OGR1** , **GPR4** , **G2A** , **1** appear to be activated by **SPC**, **LPC**, **psychosine** and/or protons. [2007]

Identification of **T cell** death-associated gene 8 (**TDAG8** ) as a novel acid sensing **G-protein-coupled receptor** . [2005]

The gene, human **TDAG8** (**hTDAG8** ) , which belongs to the **G protein** [?]-coupled receptor superfamily, encodes a protein of 337 amino acids. [1998]

We conclude that members of this **GPCR** [?] group exhibit differential sensitivity to extracellular protons, and that expression of **TDAG8** [?]  by immune cells may regulate responses in acidic microenvironments. [2005]

In particular, **dexamethasone** caused **down-regulation** of genes promoting DP thymocyte survival (e.g., **Notch1** suppressor of cytokine signaling 1, and inhibitor of DNA binding 3) or modulation of genes activating **cell death** through the **ceramide** pathway (**UDP-glucose ceramide glucosyltransferase**, **sphingosine 1-phosphate phosphatase**, **dihydroceramide desaturase**, **isoform 1**, and **G protein-coupled receptor 65**) or through the mitochondrial machinery. [2006]

Please cite the use of iHOP as "Hoffmann, R., Valencia, A. A gene network for navigating the literature. Nature Genetics 36, 664 (2004)" and as <http://www.ihop-net.org/>.

Special thanks to Chris Sander for his continuing support.

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Links

The glucocorticoid-induced gene tdag8 encodes a pro-apoptotic G protein-coupled receptor whose activation promotes glucocorticoid-induced apoptosis.**Malone MH, Wang Z, Distelhorst CW.**

Department of Medicine, Comprehensive Cancer Center, Case Western Reserve University School of Medicine, 10900 Euclid Ave., Cleveland, OH 44106, USA.

The apoptotic action of glucocorticoids on lymphocytes makes them effective therapeutics for many lymphoid malignancies. Although it is clear that glucocorticoid-induced apoptosis requires transcription, the gene products that induce apoptosis remain unknown. Using gene expression profiles of lymphoma cell lines and primary thymocytes treated with the synthetic glucocorticoid dexamethasone, we discovered that induction of tdag8 (T-cell death-associated gene 8) was a common event in each model system investigated. Activation of TDAG8 by its agonist psychosine markedly enhanced dexamethasone-induced apoptosis in a TDAG8-dependent manner. Expression of a TDAG8-GFP fusion protein was sufficient to induce apoptosis, and repression of endogenous TDAG8 using RNA interference partially inhibited dexamethasone-induced apoptosis. Together, these data suggest that TDAG8 is a regulator of glucocorticoid-induced apoptosis and that agonists of TDAG8 may be promising agents to improve the efficacy of glucocorticoids for the treatment of leukemia and lymphoma.

PMID: 15485889 [PubMed - indexed for MEDLINE]

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Normal immune development and glucocorticoid-induced thymocyte apoptosis in mice deficient for the T-cell death-associated gene 8 receptor. [Mol Cell Biol. 2006]

Critical function of T cell death-associated gene 8 in glucocorticoid-induced thymocyte apoptosis. [Apoptosis. 2003]

Thioredoxin-interacting protein (txnip) is a glucocorticoid-regulated primary response gene involved in mediating glucocorticoid-induced apoptosis. [Oncogene. 2006]

TDAG8 is a proton-sensing and psychosine-sensitive G-protein-coupled receptor. [J Biol Chem. 2004]

The pro-apoptotic protein Bim is a convergence point for cAMP/protein kinase A- and glucocorticoid-promoted apoptosis of lymphoid cells. [J Biol Chem. 2004]

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1: Fukunaga S, Setoguchi S, Hirasawa A, Tsujimoto G.

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Monitoring ligand-mediated internalization of G protein-coupled receptor
as a novel pharmacological approach.

Life Sci. 2006 Dec 3;80(1):17-23. Epub 2006 Aug 25.

PMID: 16978657 [PubMed - indexed for MEDLINE]

2: Malone MH, Wang Z, Distelhorst CW.

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The glucocorticoid-induced gene tdag8 encodes a pro-apoptotic G protein-
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apoptosis.

J Biol Chem. 2004 Dec 17;279(51):52850-9. Epub 2004 Oct 12.

PMID: 15485889 [PubMed - indexed for MEDLINE]

3: Murakami N, Yokomizo T, Okuno T, Shimizu T.

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G2A is a proton-sensing G-protein-coupled receptor antagonized by
lysophosphatidylcholine.

J Biol Chem. 2004 Oct 8;279(41):42484-91. Epub 2004 Jul 27.

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